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Patent
212/083

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **HOGAN, et al.**	Group Art Unit 1809
Serial No. 08/454,529	Examiner MARSCHEL, A.
Filed: May 30, 1995	
For: METHODS FOR SELECTING NUCLEOTIDE SEQUENCES FOR THE DETECTION AND/OR QUANTITATION OF NON-VIRAL ORGANISMS	

37 C.F.R. § 1.131 Declaration of James John Hogan, Richard Dana Smith, JoAnn Kop Dileanis (formerly JoAnn Kop), and Sherrol Hoffa McDonough

Assistant Commissioner for Patents
Washington, D.C. 20231

We, James John Hogan, Richard Dana Smith, JoAnn Kop Dileanis, and Sherrol Hoffa McDonough declare as follows:

1. Prior to September 11, 1987, we conceived and reduced to practice the use of a "hot spot" variable region located in a position approximately corresponding to bases 980-1050 of *E. coli* 16S rRNA (hereinafter the "980-1050 rRNA region") for detecting different organisms or groups of organisms. A hot spot variable region potentially contains a nucleic acid sequence specific, or unique, for different organisms or groups of organisms. Oligonucleotide probes for detecting a particular organism or group of organisms can be designed by targeting such unique sequences within a variable region.

2. The 980-1050 rRNA region was identified as a hot spot variable region based on a sequence alignment of different bacteria. It was understood that the complement thereof, for example, as found in DNA encoding the rRNA, has the same uniqueness.

3. Evidence illustrating the reduction to practice of the use of the 980-1050 rRNA region for detecting whether different organisms or groups of organisms may be present in a sample is provided, for example, in prior application U.S. Serial No. 07/083,542 (the '542 application) and Exhibits A and B (attached hereto).

4. The '542 application illustrates the use of the 980-1050 rRNA region for detecting Legionella. The '542 application was filed on August 7, 1987, and is an ancestor of the present application. Probe 3 described on page 48 of the '542 application is described on page 61 of the present application. Probe 3 is directed to a Legionella rRNA sequence found in a location corresponding to bases 975-1020 of *E. coli* 16S rRNA. Page 48, lines 4-6, of the '542 application indicates that probe 3 is specific for the genus Legionella. Pages 49-50 of the '542 application provide data illustrating the ability of a probe mix containing probe 3, along with two other Legionella probes, to be specific for Legionella organisms.

5. Exhibit A illustrates the use of the 980-1050 rRNA region for distinguishing *Mycobacteria tuberculosis* from phylogenetically closely related organisms. The Mycobacterium probe used in Exhibit A was designated MchA 1026. Exhibit B, attached hereto, is an oligonucleotide request form providing the sequence of MchA 1026. The MchA 1026 oligonucleotide was requested and synthesized prior to September 11, 1987. The dates from Exhibit B were redacted. In the

present application, the MchA 1026 oligonucleotide is described on page 50, line 26, to page 51, line 11, and is designated probe 1. The MchA 1026 oligonucleotide is directed to a Mycobacterium 16S rRNA sequence located in a position corresponding to bases 1025-1060 of *E. coli* 16S rRNA.

6. Exhibit A contains notebook pages 49 and 50. The experiments shown in Exhibit A were carried out prior to September 11, 1987, by employees of Gen-Probe Incorporated, under the supervision and at the direction of one or more of the declarants listed above. The dates were redacted from Exhibit A. The experimental protocol used in Exhibit A is provided on notebook page 49. "HA" refers to hydroxyapatite and "PB" refers to phosphate buffer. The results provided on notebook page 50 demonstrate the ability of the MchA 1026 oligonucleotide to distinguish M. tuberculosis rRNA (Mtb) nucleic acid from *C. xerosis* rRNA (Cxe), *N. asteroides* rRNA (Nas), *N. otitidis-caviarum* rRNA (Not-cav), and *R. bronchialis* rRNA (Rbr). A control with no nucleic acid was also used in the experiment ("LNC").

We hereby declare that all statements made herein of our own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so

made, are punishable by fine or imprisonment, or both, under Section 1001, of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application and any patent issuing thereon.

Date: March 2, 1998 By: James John Hogan
James John Hogan

Date: _____ By: _____
Richard Dana Smith

Date: _____ By: _____
JoAnn Kop Dileanis
(formerly JoAnn Kop)

Date: March 2, 1998 By: Sherrol Hoffa McDonough
Sherrol Hoffa McDonough